بسم الله الرحمن الرحيم

والحمد لله رب العالمين والصلاة والسلام علي أشرف المرسلين سيدنا محمد النبي الأمي الهادي الأمين وعلي آله وصحبه أجمعين...

وبعـــــد

والله إني أحبكم في الله ....

وأدعو الله أن يجمعنا بهذا الحب في ظل عرشه يوم لاظل إلا ظله

فهذا تلخيص مختصر لأهم موضوعات الخلل في التمثيل الغذائي ...

Inborn Errors of Metabolism

راجيا من الله سبحانه وتعالي ان ينفعنا واياكم به وأن يكتب لنا ولكم النجاح في الدنيا والأخرة ..

ولنعلم جميعا أن النجاح هو رزق من الله سبحانه وتعالي يهبه لمن يشاء وقتما يشاء . ولكن هو فقط من باب الأخذ بالأسباب

ربنا تقبل منا إنك أنت السميع العليم وتب علينا إنك أنت التواب الرحيم.

أخوكم د. محمد السعيد

Phenylketonuria

Definition:

AR disease ccc by ↑ phenylalanine > 20 mg/dl due to ↓ in phenylalanine hydroxylase.

Normally:

Phenylalanine —(Phenylalanine Hydroxylase)→ Tyrosine

بالتالي لما الانزيم يقل ... الفينيل الانين يزيد... والتيروزين يقل ....

C/P :

- **Normal** at birth
- **CNS**: seizures, microcephaly , tremors, MR.
- **Skin**: light skin, Eczema, hair loss & blond (أشقر) and blue eyes.

Investigations:

- Neonatal screening: → Bact. inhibition test & TMS
- ↑ Plasma phenylalanine.
- EEG abnormalities.
- Prenatal diagnosis.

TTT:

- Diet restricted with phenylalanine **for life** .
- Give tyrosine .
- Oral BH4 →↓ phenylalanine.

Tyrosinemia

Definition:

AR defect in fumaryl aceto acetate hydrolase → ↑ Succinyl acetone → organ damage.

C/P:

- **Liver** : (Hepatomegaly, jaundice, PHT, ascites, edema of LL, coagulopathy, ↓ glucose, Liver cell failure.
- **↑ Methionine** رائحة الكباب المحروق
- **Kidney**: RTA, Rickets.
- **PN** : Pain, paralysis.

Investigations:

- ↑ Succinyl acetone (in blood, urine).
- ↑ alfa fetoprotein. **يزيد بالألاف**
- Antenatal diagnosis.
- Nronatal screening.
- LFT& KFT.

TTT

- Diet (decrease phenylalanine & tyrosine)
- Liver transplantation.

اللهم صل وسلم وبارك علي سيدنا محمد

Alkaptonuria

Definition :

AR ↓ in homogentistic acid deoxygenase → ↑ Homogentistic acid → tissue damages.

C/P :

- **Black urine on standing.**
- Darkening of tissues (ear, sclera.)

Investigation:

- ↑ Homogentistic acid in urine.

TTT :

Diet ↓ phenyl alanine, tyrosine.

Tyrosine hydroxylase deficiency

Definition:

AR ↓ of Tyrosine hydroxylase deficiency → ↓ DOPA.

Tyrosine —(Tyrosine Hydroxylase)→ DOPA

يبقي لما الانزيم يقل ال دوبا كمان يقل

C/P:

- Parkinsonism , Dystonia , Hypertonia.

Investigations:

- ↓ dopamine in C.S.F.

TTT:

- DOPA administration.

Albinism

Definition :

AR ↓ of tyrosinase enzyme that convert tyrosine to melanin → absence of melanin pigment of the skin, hair, eyes (complete or partial.)

Types :

- Partial, complete.
- Oculocutaneous, ocular and localized.

C/P :

Skin:

- lack of skin pigment
- sun burn
- skin cancer

Eye :

- photophobia
- ↓ Visual acuity
- nystagmus

Ear:

- Response to ototoxic drugs

TTT:

- Avoid sun exposure
- Use of sun screen

اللهم صل وسلم وبارك علي سيدنا محمد

Homocystienuria

Definition :

AR defect in cystathionine systhase.

Hemocystine —↓↓ SS→ cystathionine

C/P :

- **CNS** : MR & irritability.
- **Bone :** Arachnodactly & Pectus excavatum & Kyphoscoliosis and Osteoperosis.
- **Eye** : Myopia & downward Lens dislocation.

Investigations:

- ↑ Homocystein in urine.

TTT:

- diet ↓ in methionine.
- B6, folic acid.



Hartnup disease

Definition :

- AR defective intestinal absorption of tryptophan.
- Tryptophan is important in formation of niacin. Its deficiency → niacine deficiency

C/P

Skin → photosensitivity , rash and eczema

C.N.S → atoxia, depression

GIT → glossitis

Others → blue diabrer syndrome

Investigations:

↑ urine neutral amina acids (as Tryptopha, pheyl alanie, tyrosine ….etc.)

Treatment:

nicotinic acid. **لانه هو الناقص في الجسم**

اللهم صل وسلم وبارك علي سيدنا محمد

Urea cycle & Hyperammonemia

The function of urea cycle is to get rid of NH_3. So, any defect in urea cycle leads to ↑ of NH_3.

C/P:

- **Neonates :** Poor feeding ,vomiting , FTT and hepatomegaly,
- **Infants** : Lethargy, coma, convulsion.

Investigations:.

- ↑ NH_3 , ↑ ALT, ↑ AST.
- ABG → Resp. alkalosis.

TTT:

1- ↑ IV fluid, glucose 10%.

2- ↓ protein in diet.

3- ↑ NH_3 excretion by (Na benzoate , phenyl acetate , argenine.)

4- Renal analysis.

5- Neomycin →↓ production of NH_3.

6- Lactulose →↓ absorption of NH_3.

اللهم صل وسلم وبارك علي سيدنا
محمد وعلي آله وصحبه أجمعين

Maple Syrup Urine Disease

Definition:

AR deficiency of α ketoacid dehydrogenase → defect of metabolism of essential amino acids valine, Isoleucin, leucin (V I L)

C/P:

- Poor feeding, vomiting, FTT.
- Lethargy, seizures, coma.
- **Maple syrup odor of urine**.

Investigation:

- ↑ VIL in blood & urine.
- Hypo glycemia & metabolia acidosis.
- Enzyme assay.
- Neonatal screening.
- Antenatal diagnosis.

TTT:

- Iv fluida & adequate kalories.
- ↓ VIL in diet
- Renal dialysis
- Liver transplantion



Isovaleric Acidemia

Definition:

AR deficiency of iso valeryl COA dehydrogenase →↑ Iso valeric acid

C/P :

- Poor feeding, FTT vomiting ,
- lethargy , coma , seizures.
- Metabolic acidosis.

Investigation:

- Neonatal screening.
- Prenatal diagnosis.
- ABG → metabolic acidosis.
- Isovaryl COA delydroyenase.
- CBC → Neutropenia, anemia ,thrombocytopenia.

TTT:

- I.V. Fluid.
- TTT of acidosis.
- protein restriction.
- Renal dialysis.



X-linked Adrenoleukodystrophy

Definition:

X-linked defect of catabolism of very long chain fatty acids (VLCFA).

= ↑ deposition of VLCFA → C.N.S (white matter) & adrenal gland (cortex.)

Forms:

A → Asymptomatic.

A → اطفال ATFAL → childhood form.

A → Adult form.

A → Adrenomyelo neuropathy.

A → Adisson only.

C/P

→↑ ACTH → hyperpigmentation of skin.

→ C.N.S symptoms →↑ ICP, bulbar symptoms.

→ Adrenal cortex → adrenal insufficiency.

Investigations:

- ↑ VLCFA in blood.
- CT, MRI for C.N.S involvement.
- Adrenal function test (cortisol, ACTH)

TTT:

- Lorenzo oil → ↓ formation of VLCFA 50%
- Adrenal Replacement.

Gaucher disease

Definition :

AR disease ccc by ↓ Glucocerebrosidase → ↑ Glucocerebrosides In RES & CNS.

C/P :

- **Type 1:** HSM & hypersplenism and pancytopenia.
- **Type 2**: HSM & neuropathic pain.
- **Type 3** : Neuropathic pain only.

Investigations:

- BM biopsy.
- enzyme assay.
- antenatal diagnosis.

TTT:

- Enzyme replacement.
- Splenectomy
- BM Transplantation.



Niemannpick disease

Definition:

AR defect of sphingo mylinase enzyme.

C/P:

Type A → HSM, neurological , cherry red spots in eye.

Type B → HSM, **No** neurological.

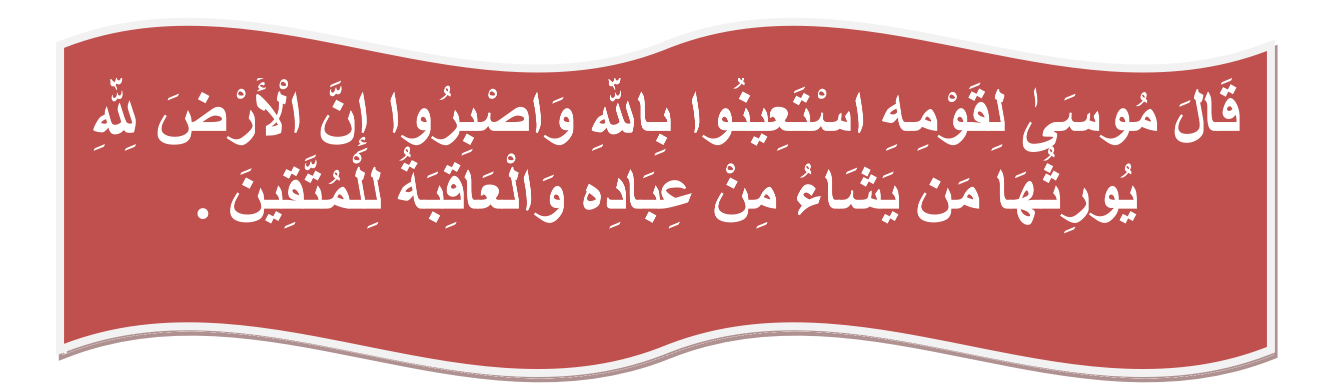
Type C → HSM, neurology (Ataxia).

Instigation:

- BM examination → foam cells.
- Enzyme assay.
- Antenatal diagnosis.

TTT:

- Enzyme replacement.
- Liver transplantation.
- Supportive ttt .



Mucopolysacchridosis (MPS)

Definition:

AR lysosomal disorder due to ↓ of degradation of GAG:

C/P:

- Normal at birth.
- Dysmorphic features
- Affection of (CNS, eye, skin , joints.)

Classification:

افتكر الجملة دي وادعي للدكتور علي غانم ...

هات شاي لعنتر ....

وعنتر عينه سليمة علشان كده عبلة حبته .

والسمك الفيلية غبي و الصيادين اصطادوه لان عنده تخلف عقلي .

ومرقص ده ولد مش مظبوط عمال بيترقص وعنده كيفوزس بس عاقل .

ومراته كمان عاقلة ...

وسالي قصيرة وعاقلة ...

بس مرضيتش برقم ٨ واتجوزت رقم ٩ اللي قصير زيها..

والباقي متخلفين ..

- **Hurler syndrome.** هات
- **Sehie syndrome.** شاي
- **Hunter syndrome.** لعنتر
- **Sanfilipo syndrome.** سمك فيليه
- **Morquio syndrome.** مرقص
- **Maroteux syndrome.** ومراته
- **Sly syndrome** سالي
- **Type 8** رفضت ٨
- **Type 9** واتجوزت ٩

Characters :

❖ **Hurler syndrome** هات

- Normal at birth.
- Nasal discharge, MR, kyphosis, HSM.
- Cardiomyopathy.
- Hydrocephalus.
- Joint stiffness.
- Corneal opacity.

❖ **Sehie syndrome:** شاي As hurler except.

- Clow hand.
- Normal mentality

❖ **Hunter syndrome:** لعنتر

- XL – recessive.
- No corneal opacity. عينه حلوة

❖ **Sanfilipo syndrome:** سمك الفيليه غبي

- Severe MR.

❖ **Morquio syndrome:** مرقص بيترقص وعنده كيفوزس بس عاقل

- Server kyptosis & flat fee & Normal mentality.

❖ **Maroteux syndrome:** ومراته كمان عاقلة

- Normal mentality.

❖ **Sly syndrome:** سالي قصيرة بس عاقلة

- Normal mentality & Short stature.

❖ **Type 8 :** لم تقبل برقم ٨ لانه عفي عليه الزمن

- No longer used.

❖ **Type 9:** وقبلت ب ٩ لانه قصير برضو

- Soft tissue mass & Short stature.

Glycogen Storage Disease

Type I: (von gerk disease):

- Marked hepatomegaly.
- Hypoglycemia.
- Hyper lipidemia.
- Hyper uric acaedemia.
- Coagulation defect.

Type II (pompe):

- Cardiomyopathy.
- Myopathy.
- Hepatomegaly.

Type III:

- Myopathy.
- Hepatomegaly.

Type IV: = Failure of liver

- severe cirrhosis.
- PHT.
- Ascites.
- HSM.

Types V:

- Muscle cramps.
- Easy fatigability.

اللهم صل وسلم وبارك علي سيدنا محمد

Galactosemia

Causes :

- Galactose 1-p Uridyl transferase.
- Galactokinase.
- Epimerase.

C/P :

- Hepatomegaly, splenomegaly, ascites.
- hypoglycemia, convulsions.
- FTT & vomiting.

Investigation :

- Enzymes assay.
- reducing substance in urine.

Treatment :

- lactose free diet.

مع تمنياتى لكم جميعا بالنجاح والتوفيق

د. محمد السعيد

